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**RADIATION INACTIVATION
OF HISTAMINE IN AQUEOUS SOLUTION
AND IN PLASMA**

ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE
Defense Nuclear Agency
Bethesda, Maryland

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July 1971

RADIATION INACTIVATION OF HISTAMINE
IN AQUEOUS SOLUTION AND IN PLASMA

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ABSTRACT

Dilute solutions of histamine in water and plasma were given 140- to 38,000-rad doses of pulsed mixed gamma-neutron radiation. Histamine activity of the solutions was bioassayed using guinea pig ileum. Inactivation of the histamine in water was apparent at doses of 2000 rads or more; 1.5 $\mu\text{g}/\text{ml}$ of histamine in water were completely inactivated by 17,300 rads, 3.0 $\mu\text{g}/\text{ml}$ required 33,000 rads. Different concentrations of histamine (1.5 to 2.7 $\mu\text{g}/\text{ml}$) receiving the same dose of radiation (17,300 rads) clearly showed an inverse relation between concentration and inactivation. Histamine in plasma showed less than 10 percent inactivation even at the highest dose used, 38,000 rads.

I. INTRODUCTION

The hemodynamic changes experienced by irradiated animals may be attributed in part to the release of histamine.^{3,6} There is some indication in monkeys, however, that early postirradiation hypotension becomes less pronounced as the dose is increased to very high values (20,000 to 30,000 rads). Some of the possible explanations for this lessened effect are: (1) the labile, nonmast cell histamine is inactivated directly or indirectly by ionizing radiation; (2) histamine receptor sites are markedly altered; and (3) other vasoactive substances are released (or their synthesis induced) which counteract the effects of histamine.

The objective of this experiment was to determine in vitro if pulsed mixed gamma-neutron radiation could inactivate histamine to an extent that the less pronounced hemodynamic effects observed in monkeys following very high doses of radiation might be explained.

II. METHODS

Histamine dihydrochloride* concentrations of 1.5 to 3.0 $\mu\text{g/ml}$ (as the base) in distilled pyrogen-free water or in pig plasma were given 140 to 38,000 rads of mixed gamma-neutron radiation (incident neutron to gamma ratio of 0.4) from the AFRRI-TRIGA reactor in a single pulse of short duration (pulse width at half maximum approximately 25 milliseconds).

The solutions were irradiated in stoppered glass test tubes but were not deaerated. The possibility of the glass adsorbing histamine was tested² and no measurable

* Fisher Scientific Company, Fair Lawn, New Jersey

adsorption was found; however, to preclude the occurrence of this possible error nonirradiated standards were handled the same as irradiated samples.

Histamine was bioassayed by the method described by Sturde and Heitmann.⁵ A 2-cm terminal ileum segment from a male guinea pig was suspended in a bath of oxygenated Tyrode's solution at 37° C. The histamine containing solutions were applied to the ileum segment and resulting contractions were measured by a linear motion transducer* and recorded.†

The sensitivity of each ileum segment was established by recording the contraction intensity following application of 0.1 ml of histamine standard having the same concentration as originally contained in the irradiated solution to be measured. After a few seconds, the strip was washed with Tyrode's solution, 0.1 ml of the irradiated solution was applied, and the resulting contraction intensity recorded. Following measurement of the irradiated sample activity, the histamine standard was again applied to the ileum strip and the contraction recorded. The two responses from histamine standard were averaged and the contraction from the irradiated sample was then expressed as a percentage of the calculated average. Each data point on Figures 1 and 2 represents the mean value of at least three such comparisons of irradiated sample to standard except where no error bar is shown.

III. RESULTS

Aqueous solutions of histamine in concentrations of 1.5 to 3.0 $\mu\text{g/ml}$ were inactivated by mixed gamma-neutron irradiation. Inactivation became apparent at

* Phipps and Bird, Inc., Richmond, Virginia

† Oscillo-riter, Texas Instruments Company, Houston, Texas

about 2000 rads; the 1.5 $\mu\text{g}/\text{ml}$ solution was completely inactivated by 17,300 rads, and the 3.0 $\mu\text{g}/\text{ml}$ solution by 33,000 rads (Figure 1).

Histamine concentrations of 1.5, 1.8, 2.1, 2.4 and 2.7 $\mu\text{g}/\text{ml}$ in water receiving 17,300 rads clearly showed an inverse relationship between concentration and inactivation (Figure 2).

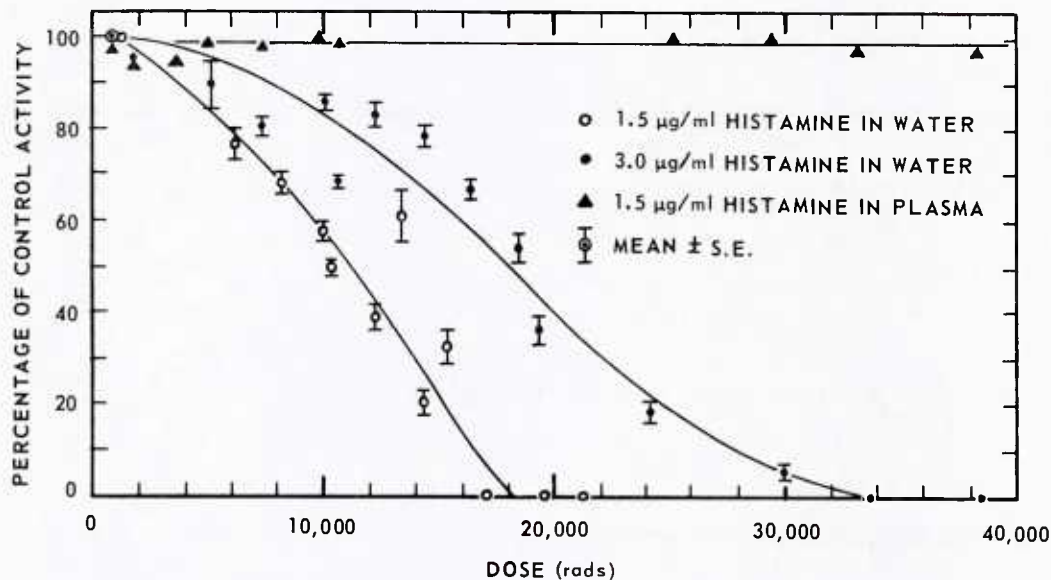


Figure 1. Histamine inactivation in water and plasma solutions after mixed gamma-neutron irradiation

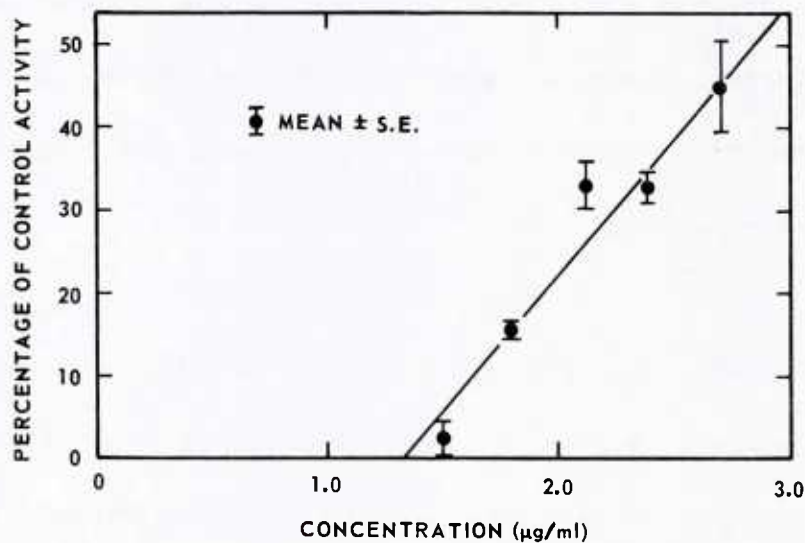


Figure 2. Activity of aqueous histamine solutions after 17,300 rads of mixed gamma-neutron irradiation

Histamine in plasma solution showed less than 10 percent inactivation even at the highest dose used, 38,000 rads.

IV. DISCUSSION

Sturde and Heitmann⁵ found that dried or frozen histamine was insensitive to inactivation by irradiation and concluded that the inactivation of histamine in aqueous solution was due to endogenously formed, radiation-derived hydroxyl radicals.

Since the aqueous solutions used in this study were very dilute, the primary effect of the absorbed energy was decomposition of water in a radical yielding process⁷



and to a lesser extent to the forward or molecular process¹



Generally the radicals and molecules formed react preferentially with organic substrate,⁴ in this instance, histamine. Histamine inactivation reflected the concentration of free radicals which increased as the dose of ionizing radiation was increased.

The concentration of other organic solutes in plasma far exceeds that of histamine and since the rate of reaction is a function of concentration, the histamine remained relatively unaffected.

V. CONCLUSIONS

Although it is evident by this and other studies⁵ that histamine in dilute aqueous solutions is inactivated by ionizing radiation, the lack of inactivation in plasma solutions weakens any conclusion that might be drawn concerning histamine inactivation in vivo playing a role in hemodynamic effects from very high doses of radiation.

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